

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Wheeler	
Application No.: 09/875,805	
Filed: 6/5/2001	
Title: Method for Preventing Aggregation of a Lipid:Nucleic Acid Complex	
Attorney Docket No.: INEX.P-010	
	Group Art Unit: 1635
	Examiner: Epps, J.L.

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Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

RESPONSE AFTER FINAL REJECTION

This is in response to the Office Action mailed March 21, 2003 for the above-captioned application.

Applicants request an extension of time to make this paper timely and enclose the fee. The Commissioner is authorized to charge any additional fees or credit any overpayments to Deposit Account No. 15-0610.

Reconsideration and further examination are respectfully requested.

Claims 1-14 are pending in this application.

The Examiner has maintained the rejection of 1-6 and 8-13, and has added claims 7 and 14 to the rejection as anticipated by Choi et al. The Examiner states that the amendment of the claims necessitated the new ground for rejection, namely the addition of claims 7 and 14 to this rejection, but has not said how this could be the case. Neither claim 7 nor claim 14 was amended or added in the amendment of January 7, 2003. Accordingly, since this Office Action presented

I hereby certify that this paper and any attachments named herein are transmitted to the United States Patent and Trademark Office, Fax number: 703-872-9307 on July 21, 2003.

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July 21, 2003
Date of Signature

a new ground for rejection which could have been made by the Examiner in the previous official action, the finality of the rejection is not proper. For this reason, withdrawal of the finality and issuance of a further official action in the event the claims are not all deemed allowable are requested.

Turning to the merits of the rejection, as previously stated the claims of the instant application are directed to a **method** for preventing particle aggregation or of making lipid:nucleic acid particle with less tendency to aggregate (claim 1) and to a method for making a lipid:nucleic acid complex (claim 8). These methods recite specific steps, and in order to anticipate the claim the Choi reference must teach the performance of these steps. The Examiner has not shown this to be the case.

Claim 1 recites that the methods comprises the step of "incorporating a non-cationic lipid into a composition comprising lipid:nucleic acid complex particles," wherein the particles comprise a cationic lipid and a nucleic acid polymer, and wherein the non-cationic lipid is a polyethylene glycol-based polymer. Claim 8 recites step (a) which is forming a lipid:nucleic acid complex, and step (b) which is mixing this complex with a non-cationic lipid. Both of these claims require a specific order of steps, i.e, the formation of a lipid:nucleic acid complex, and the subsequent addition of the non-cationic lipid.

Choi reference discloses lipid particles in which PEG-modified ceramide lipids are combined with other lipids into lipid particles. These PEG-ceramide particles are said, at Col. 4, lines 28-33, to be effective to prevent aggregation of liposomes incorporating DNA. This, however, does not amount to a teaching of the claimed method. One skilled in the art can readily imagine multiple possibilities for making PEG-ceramide-containing liposomes that incorporate DNA. The most obvious of these is making a PEG-Ceramide-containing liposome, and then adding DNA to the liposome, particularly since the discussion at Cols 17-18 of DNA delivery is based on complexation of the DNA with a lipid. This order of steps is different from that required by the present claims, which require that the PEG-Ceramide be added to a preestablished DNA:Lipid complex. Nothing in Choi teaches such an order of method steps, and thus Choi cannot be said to anticipate any of the present claims.

In the Official Action, the Examiner states that "contrary to Applicant's assertions, as stated in the prior Office Action, the PEG-modified ceramide lipids of Choi et al can be used in

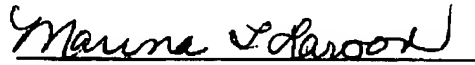
preventing aggregation of liposomes incorporating ... DNA." Applicants believe that the Examiner has failed to appreciate the argument that was being made. Applicants are not contesting that Choi teaches that if you make a liposome with PEG-ceramide in it, and then add DNA, that aggregation will be reduced. What Applicants said in the last response was that "nothing in Choi suggests that adding a PEG-modified ceramide to a pre-existing lipid:nucleic acid complex would result in any change in the aggregation behavior or any other specific property of that complex." This is a very different proposition.

One can look at the two situations graphically as shown in the attached sketch. When liposomes are preformed with a cationic lipid and PEG-ceramides, the PEG tails stick out from the liposome acting as a steric barrier. Negatively charged DNA can get down between the tails to interact with the positive charges of the cationic lipid, but is restricted in its ability to form a bridge between two liposomes because of the PEG-tails. Thus, the PEG prevents aggregation. On the other hand, when a complex of lipids and DNA is formed initially, there is nothing to prevent the polyanionic DNA from interacting with multiple positively-charged lipids. When PEG-ceramide is added to this complex, the prior art provides no indication that it would have any impact on the structure in any way.

For these reasons, Applicants again submit that claim s1-6 and 8-13 are not anticipated. With respect to claim 7 and 14, the Examiner asserts that the "gene construct" referred to in claim 16 of Choi "encompasses the vectors recited in claims 7 and 14 of the instant application." Applicants respectfully request clarification of this argument if the rejection is maintained, since merely being encompassed by something is not sufficient for a conclusion of anticipation. Many things that are dominated by earlier claims, i.e., encompassed, are subsequently found to be patentable because they are not specifically disclosed.

In view of the foregoing, Applicants submit that the application, as amended, is in form for allowance. Favorable reconsideration and allowance of all claims are respectfully urged.

Respectfully Submitted,



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